UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/463,082	07/10/2000	CHENICHERI H. NAIR	5-00	5840

23713 7590 07/14/2003

GREENLEE WINNER AND SULLIVAN P C
5370 MANHATTAN CIRCLE
SUITE 201
BOULDER, CO 80303

EXAMINER	
WELLS, LAUREN Q	
ART UNIT	**PAPER NUMBER**
1617	23

DATE MAILED: 07/14/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/463,082	Applicant(s) NAIR ET AL.	
	Examiner Lauren Q Wells	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31-79* is/are pending in the application.

4a) Of the above claim(s) *32,36-60,62,63,65-67,69,70 and 73-79* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31,33-35,61,64,68,71 and 72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 31-79 are pending. Claims 32, 36-60, 62-63, 65-67, 69-70 and 73-79 are withdrawn from consideration, as they are directed toward non-elected subject matter.

Applicant's arguments and declaration, with respect to claims 31, 33-35, 61, 64, 68 and 71-72, have been considered but are moot in view of the new ground(s) of rejection.

Election/Restrictions

Applicant's election with traverse of the Lack of Unity Requirement in Paper No. 23 is acknowledged. The traversal is on the ground(s) that Applicant has a special technical feature.

Applicant argues, "the colloids of the present invention comprise carbonaceous particles dispersed in an aqueous medium. The combination of (i) selective binding and (ii) stable association with an aqueous media exhibited by the diagnostic and therapeutic particles of the present invention provide 'a technical relationship. . .involving one or more of the same or corresponding technical features. . .that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art". This argument is not persuasive. The Examiner respectfully points out that in the instant case the technical feature is a detectable reagent encased in at least two layers of carbon, wherein the outer surface of said particles allows for a stable chemical association with an aqueous medium. Regarding (i) and (ii) discussed by Applicant above, the Examiner respectfully points out that (i) and (ii) are properties of the technical feature. Since Watson teaches a detectable reagent encased in at least two layers of carbon, wherein the outer surface of said particles allows for a stable chemical association with an aqueous medium, the instant invention does not comprise a special technical feature, but only a technical feature.

Applicants argue, "Applicant submits that searching for prior art relevant to all of claims of Groups I-IV does not present a significant burden because the pending claims are linked by a specific and well defined technical feature". This argument is not persuasive, as there is a significant burden as Groups I-IV are each distinct inventions. In vivo methods, in vitro methods, methods of targeting drugs, and compositions are distinct inventions. To search of these claims at together, would constitute a serious burden.

Regarding Applicant's arguments towards Burch et al., the Examiner respectfully points out that Watson, as applied under 35 USC 103 below, teaches Applicant's technical feature.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 72 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(i) The term "lyophilic" in claim 72 is vague and indefinite. Webster's Dictionary defines lyophilic as marked by strong affinity between a dispersed phase and the liquid in which it is dispersed. What is a strong affinity? Does it mean that the dispersed phase never falls out of solution? Does it mean that it has a stability, i.e. no falling out of solution, for a certain period of time? The specification does not define this phrase and one of ordinary skill in the art would not be apprised of its definite meaning.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 31, 33, 34, 61 and 71 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watson et al. (WO 93/15768) in view of Koruga (5,640,705) and in view of Reno et al. (5,217,705).

The instant invention is directed toward a method for the in vivo detection of fibrin, comprising administering to a patient an effective amount of a detectable reagent comprising discrete particles dispersed in a pharmaceutically or veterinarily acceptable carrier, diluent, excipient, adjuvant or any combination thereof, wherein said particles comprise a detectable marker encased in at least two layers of carbon, wherein the outer surface of said particles allows for a stable chemical association with an aqueous medium and wherein upon administration of said regent said particles are dispersed in the aqueous medium and form a stable colloid; binding said particles to said fibrin; and detecting the presence of said detectable marker in said patient.

Watson et al. teach the use of fullerenes in diagnostic and/or therapeutic agents, especially diagnostic imaging contrast agents. The fullerenes are useful as supports or surrounds for diagnostic or therapeutic entities. The skeleton structure of the fullerenes can be derivatized to enhance other properties of the macromolecule, such as hydrophilic or lipophilic groups, or biologically targeting groups or structures. Specific derivatization groups include proteins, antibodies, cell adhesion molecules and others. Solubilizing groups can be attached to the

carbon skeleton, for example polyalkoxylated alkyl or alkoxy groups. A method of diagnostic imaging is taught, wherein a compound comprising a contrast agent in combination with a fullerene is administered to a human. Administration to the circulatory system is taught, wherein the compound targets the blood pool. The compounds are taught in physiologically acceptable carriers in the form of dispersions, which are synonymous to colloids. The reference lacks binding to fibrin and two layers of carbon. See pg. 1, 3-12, 14, 23, 26-30.

Koruga teach that fullerenes come in the form of C60, onions, nanotubes, and capsules, wherein capsules, nanotubes and onions can be formed as concentric multi-layer carbon cages. See abstract; Col. 3, lines 31-49.

Reno et al. teach a method of diagnosing blood clots using fibrin-binding proteins. The proteins are attached to detectable substances, such as radioisotopes of iodine, bromine, fluorine, or 99mTc. See Col. 5, lines 20-56.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to teach the fullerenes of Watson as comprising two or more carbon layers, as taught by Koruga, because of the expectation of achieving a product, wherein the contents of the fullerene are more fully trapped and not as susceptible to leaking out of the carbon skeleton matrix, thereby forming a more sustained-release formulation.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to teach fibrin-binding proteins, as taught by Reno et al., as the proteins of Watson et al. because Watson et al. teach their agents for targeting the blood pool and because of the expectation of achieving a stable contrast agent that is able to locate harmful fibrin blood clots.

It is respectfully pointed out that it would have been obvious to one of ordinary skill in the art to hydrolyze the outer layer of the graphite particle because of the expectation of achieving a product that is soluble in its delivery medium.

Claim 64 is rejected under 35 U.S.C. 103(a) as being unpatentable over Watson et al. in view of Koruga and in view of Reno et al. as applied to claims 31, 33, 34, 61 and 71 above, and further in view of The Handbook of Cosmetic Science and Technology.

Watson et al., Koruga, and Reno et al. fail to teach nanocolloids.

The Handbook of Cosmetic Science and Technology teaches the surface chemistry of colloid systems. It is taught that a reduction in size of the dispersed phase particles increases the stability of the colloid. See pages 67-69.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to teach the dispersion of the combined references as a nanodispersion, wherein a dispersion is a form of a colloid, because of the expectation of achieving a more stable formulation.

Claim 68 is rejected under 35 U.S.C. 103(a) as being unpatentable over Watson et al. in view of Koruga and in view of Reno et al. as applied to claims 31, 33, 34, 61 and 71 above, and further in view of Park et al. (5,330,768) and Penfold et al. (J. Phys. Chem.).

Watson, Koruga, and Reno et al. are applied as discussed above. The reference lacks C16EO6.

Park et al. teach films for drug delivery comprised of poly(lactic acid) and polyethyleneoxide and polypropylene oxide. It is taught that the water content of the polymer can be controlled by blending different kinds of block polymers and by adjusting ratios. These

compounds also exhibit a wide range of hydrophilicity/hydrophobicity. See Col. 3, line 4-line 50.

Penfold et al. teach C16EO6 as a known, beneficial nonionic polyethylene oxide surfactant. See abstract and page 18133.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to teach the polymers taught by Park et al. as the alkyl alkoxylated surfactants of the combined references because a) Park et al.'s surfactants are alkyl alkoxylated and because of the expectation of achieving a contrast agent particle compound whose hydrophilicity/hydrophobicity can be altered.

While Park et al. does not specifically teach the empirical formula C16EO6, the Examiner respectfully points out that it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. In re Aller, 105 USPQ 233. Thus, one of skill in the art would be motivated to alter the chain length of the polyethyleneoxide to obtain a surfactant with beneficial solubility properties, so as to obtain a surfactant as taught by Penfold et al.

Claim 35 is rejected under 35 U.S.C. 103(a) as being unpatentable over Watson et al. in view of Koruga and in view of Reno et al. as applied to claims 31, 33, 34, 61 and 71 above, and further in view of Doherty et al. (5,952,321).

Watson, Koruga, and Reno et al. are applied as discussed above. The reference lacks glucose in water.

Doherty et al. teach water, Ringer's solution, glucose in water, and isotonic sodium chloride, as acceptable vehicles for in vivo administration of active agents. See Col. 18, line 57-Col. 19, line 9.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the glucose in water, taught by Doherty et al., for the vehicles taught by the combined references because the combined references water, sodium chloride injections, and Ringer's solution as interchangeable vehicles, and Doherty et al. teach water-in-glucose as an interchangeable vehicle with water, sodium chloride injections, and Ringer's solution. Thus, substituting one for the other would be expected to achieve similar vehicle effects.

While Doherty et al. does not teach the glucose in an amount of 5%, it is respectfully pointed out that it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. In re Aller, 105 USPQ 233. Furthermore, one of skill in the art would be motivated to adjust the amount of glucose to be compatible with the physiological environment of the body.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lauren Q Wells whose telephone number is (703) 305-1878. The examiner can normally be reached on M-F (7-5:30), with alternate Mondays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (703)305-1877. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

lqw
June 27, 2003

SREENI PADMANABHAN
PRIMARY EXAMINER

6/27/03